Compliance Update and CBER's Regulatory Direction

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James S. Cohen, J.D.

Associate Director for Compliance and Biologics Quality
Center for Biologics Evaluation and Research

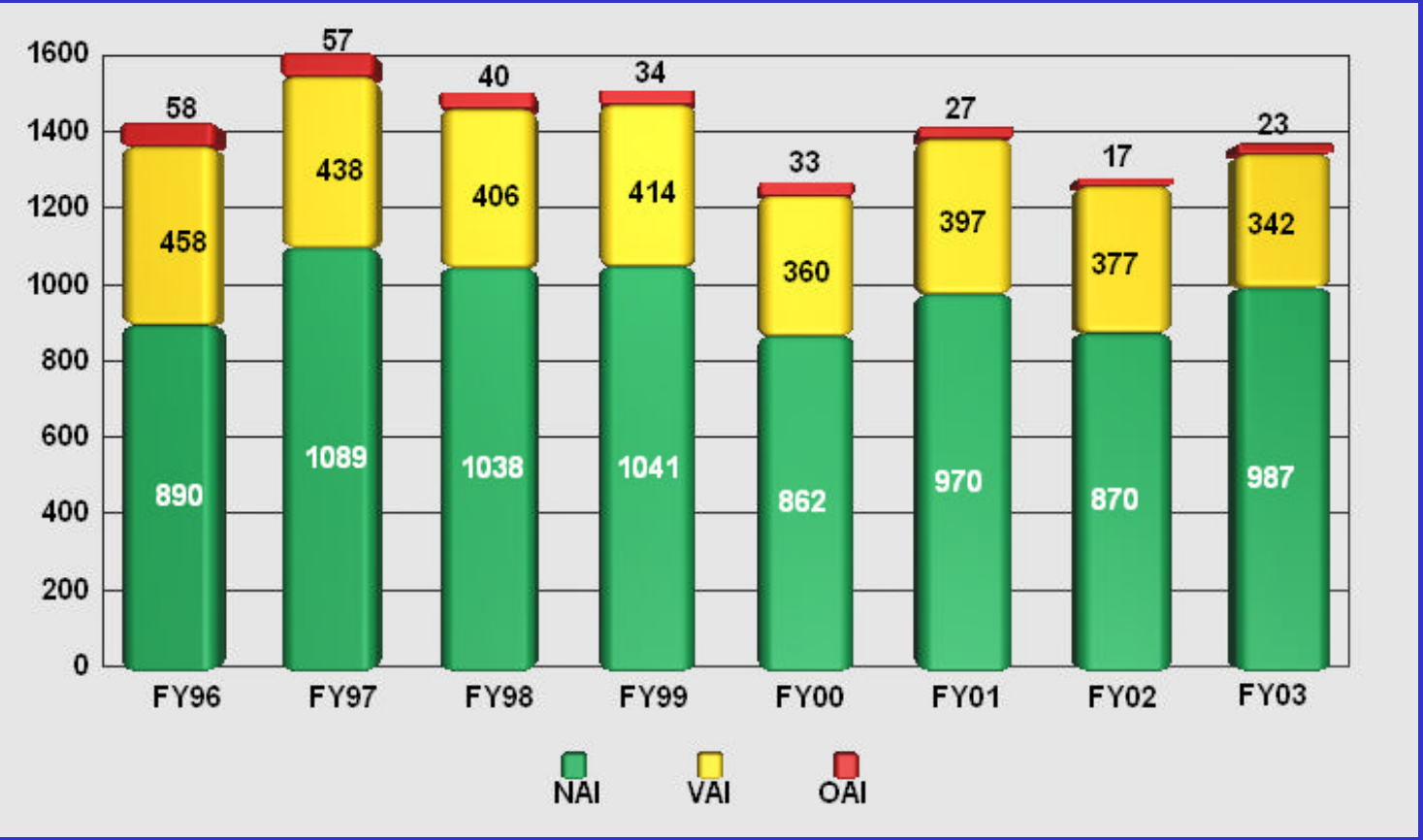
Agenda

- Compliance Data and Trends
  - Inspection and Compliance Charts
  - Biological Product Deviation Reports
  - Recalls
- Systems-Based Inspections – Risk-Based Strategies

FDA Inspection Classification System

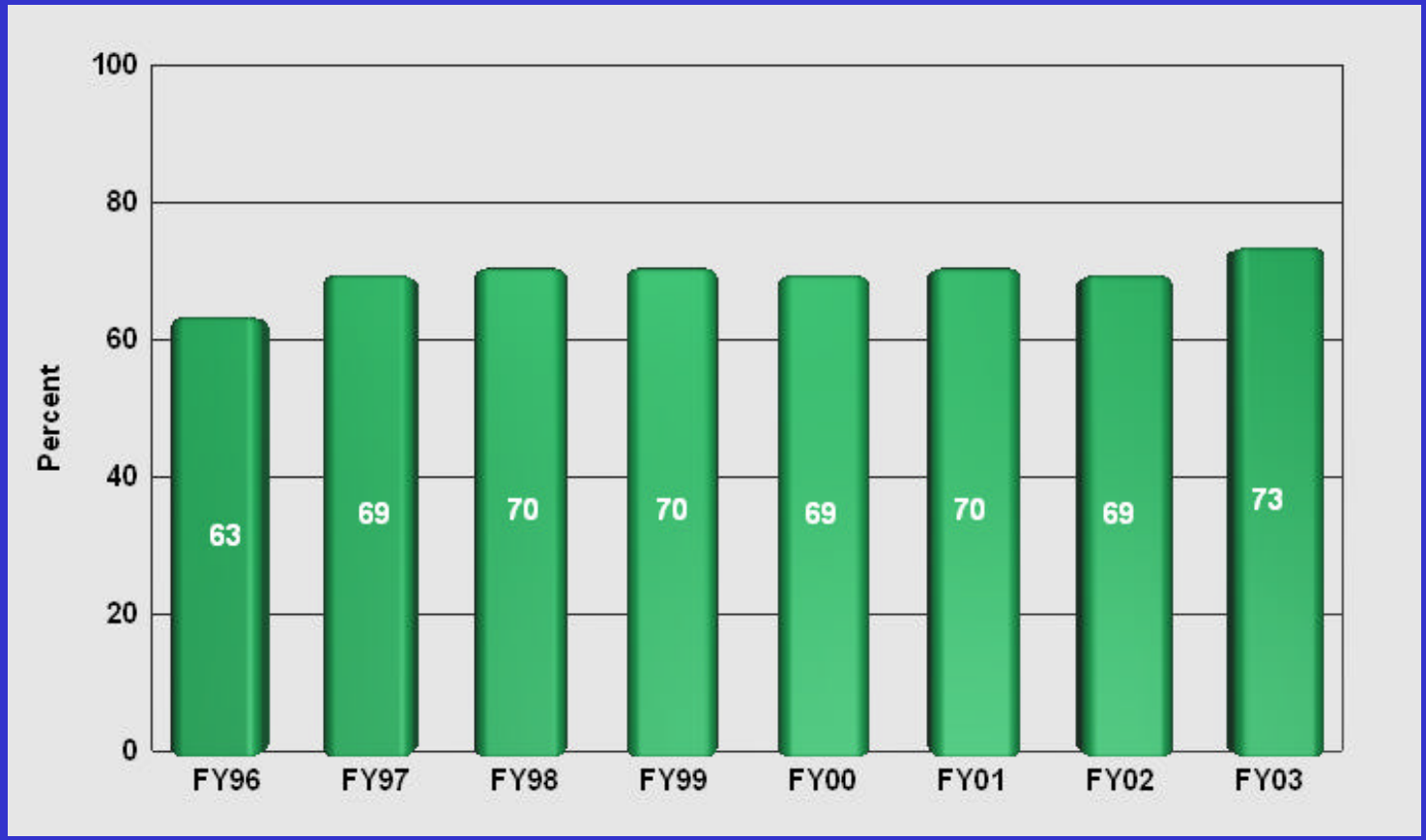
- NAI - No Action Indicated
- VAI - Voluntary Action Indicated
- OAI - Official Action Indicated

Blood
Inspection Classifications



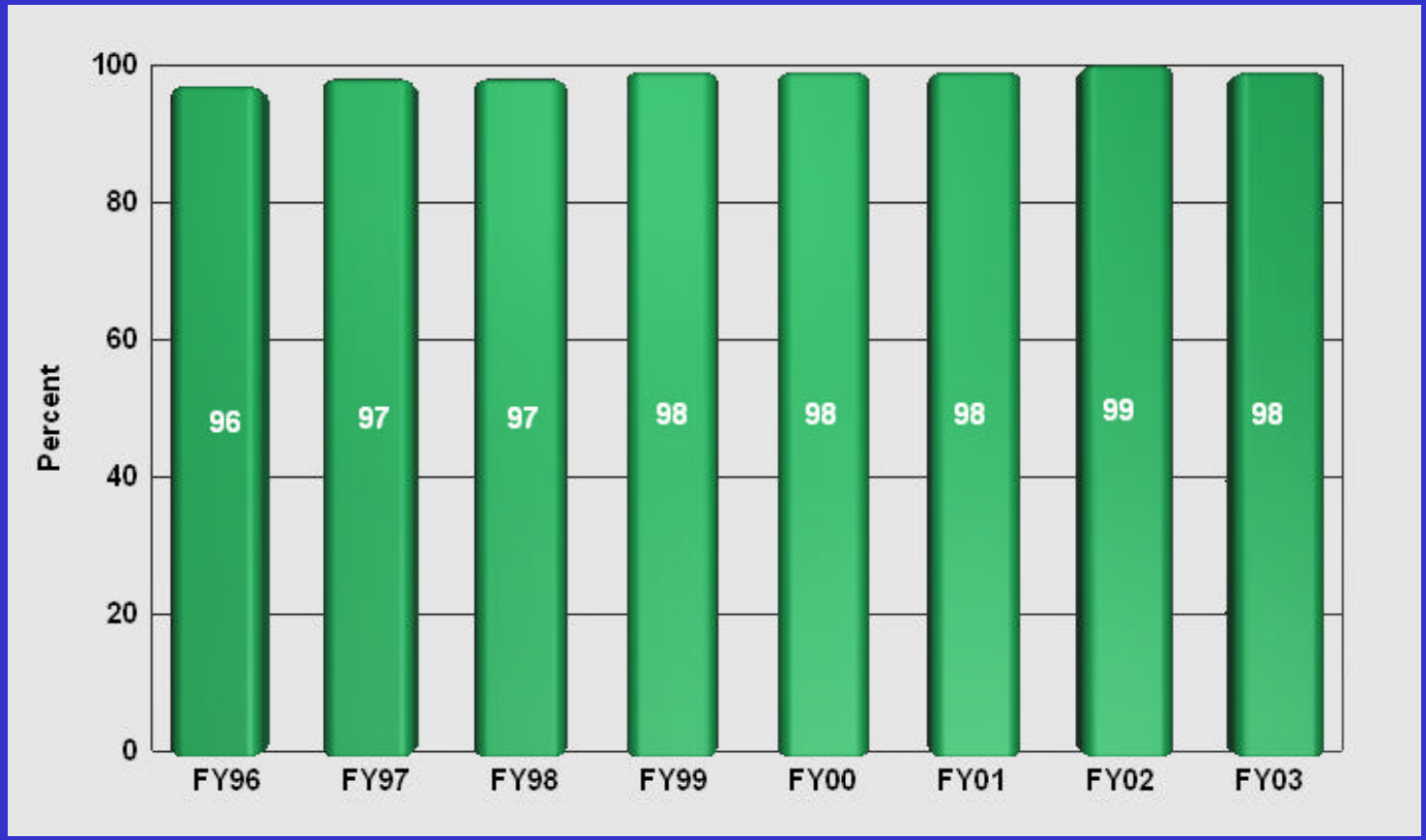
Blood Compliance Rate

NAI Inspections

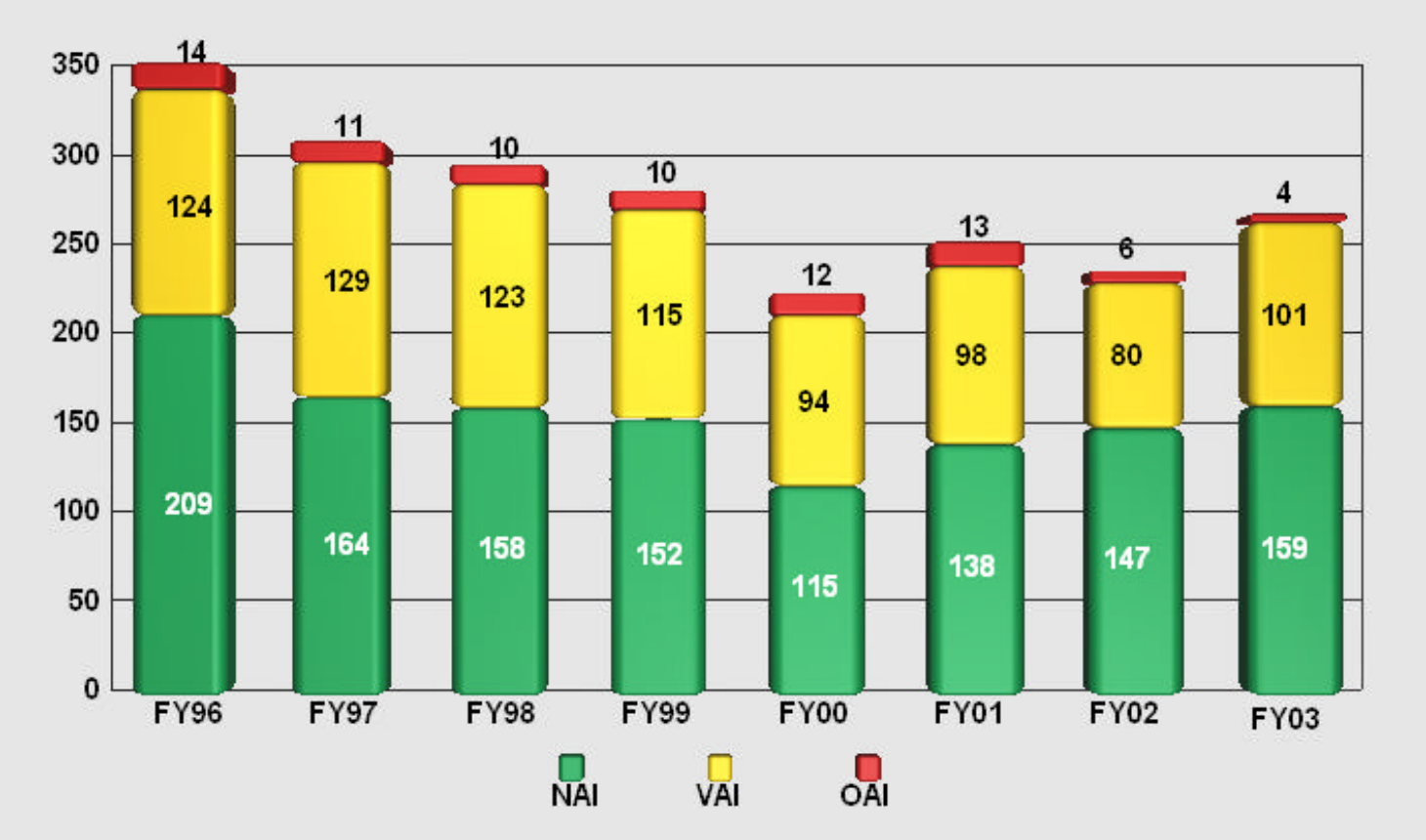


Blood Compliance Rate

NAI + VAI Inspections

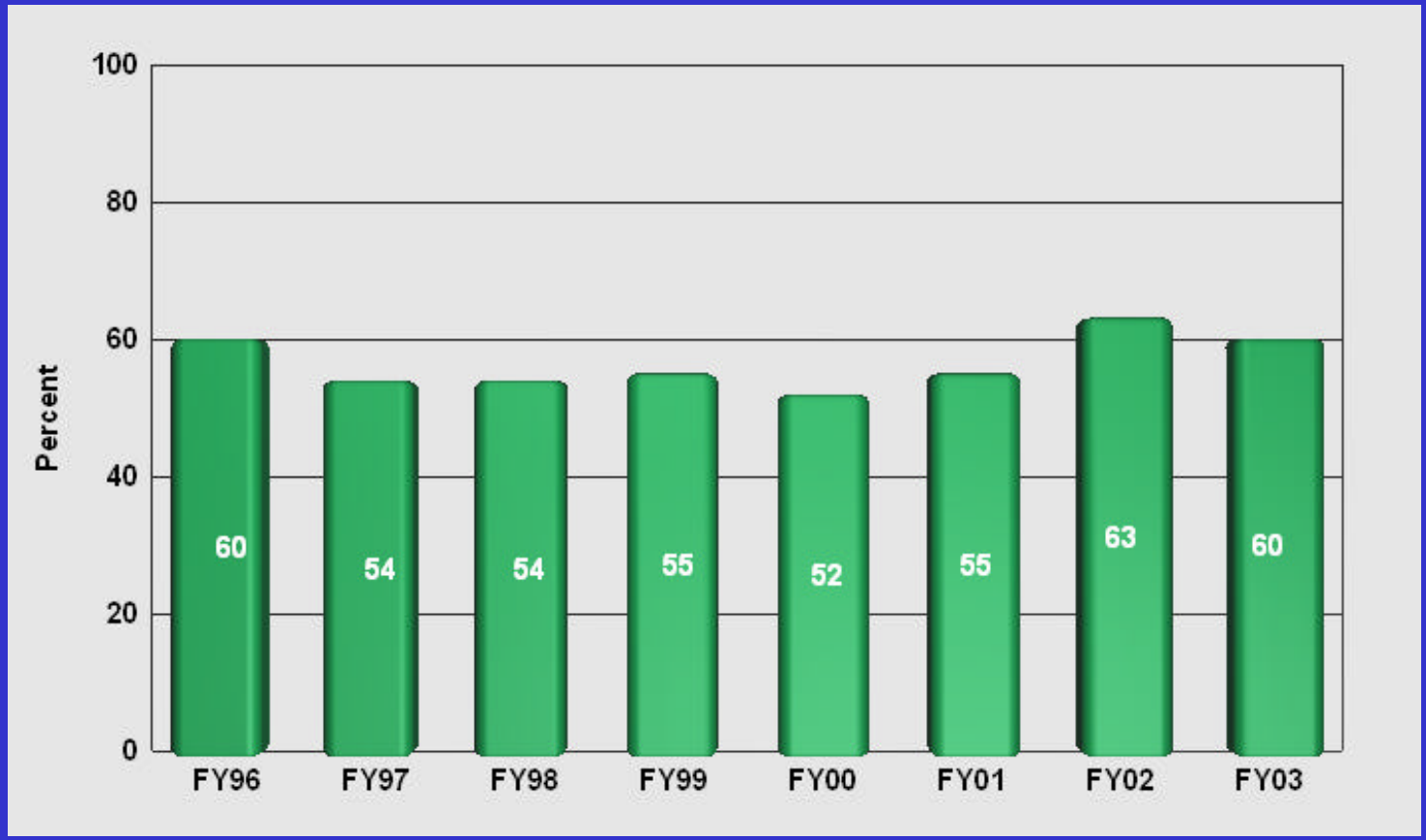


Source Plasma Inspection Classifications



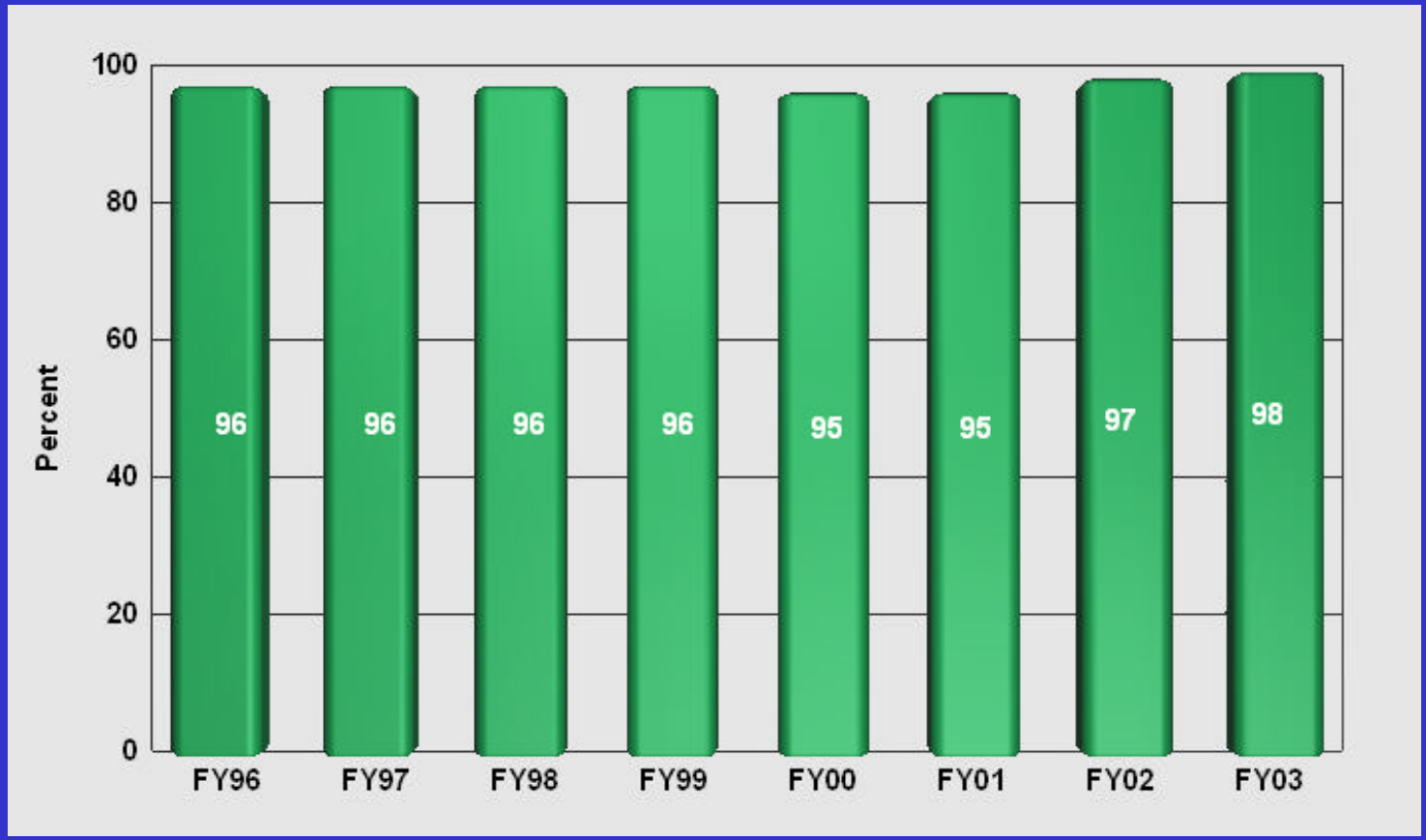
Source Plasma Compliance Rates

NAI Inspections



Source Plasma Compliance Rates

NAI + VAI Inspections



What Do These Compliance Data Mean?

- OAI classification rate generally declining (i.e., some improvement)
- NAI+VAI compliance rates appear to be improving but continue to fluctuate
- Impact of consent decrees and increased focus on CGMP compliance

Administrative and Judicial Actions

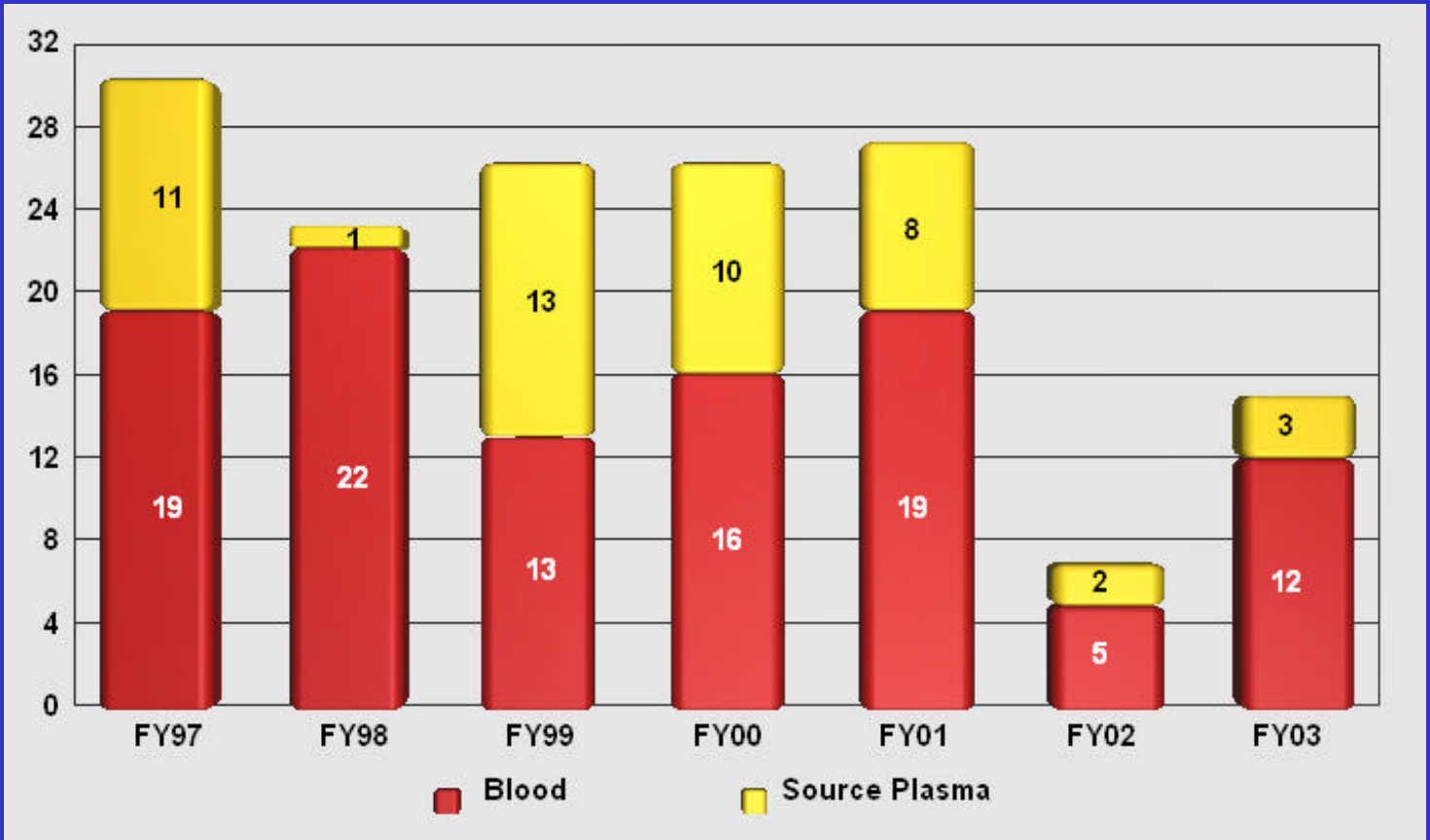
- Warning Letters
- Suspension
- Revocation
- Seizure
- Injunction

Warning Letters

- Deviations determined to be so significant as to warrant potential enforcement action
- Notification to manufacturer
- Prompt correction

Warning Letters

Blood and Source Plasma



License Suspension

- 21 CFR 601.6
- Grounds for revocation exist and danger to health
- Prohibits interstate distribution
- Requires notice to selling agents and distributors with documentation of notice to CBER
- Proceed to revocation, or possibility of resolution
- May be company-wide or site specific

License Revocation

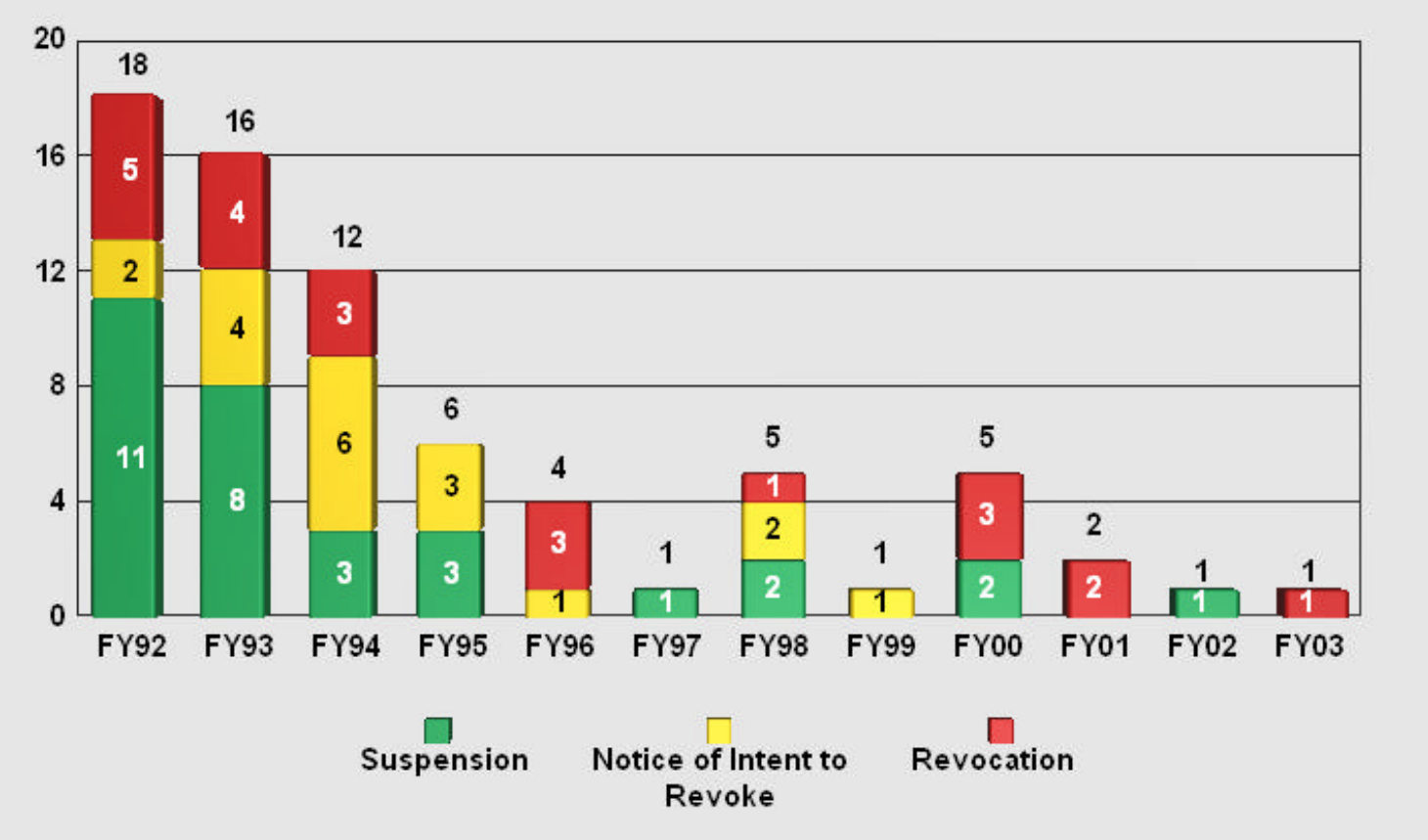
- 21 CFR 601.5
- Discontinuation of manufacturing
  - Manufacturer request for revocation
  - Revocation initiated by FDA
- Failure to report manufacturing change
- CGMP deficiencies
- New method of manufacturing
- Product not safe and effective for intended use(s)/misbranded
- May request hearing

Types of Revocation

- Notice of Intent to Revoke
  - Continuing, significant deficiencies
  - Prior warnings
  - Opportunity to correct and achieve compliance ("reasonable period")
  - If compliance not demonstrated, notice of opportunity for hearing (unless waived)
- Direct Revocation
  - In cases involving willfulness, FDA will proceed directly to revocation
  - No further opportunity to demonstrate compliance

Administrative Actions

Blood and Source Plasma



Seizure

- Removes product from market
- Not often used for blood/plasma products due to short expiration dates, industry recognition of risk, recall procedures, etc.

Injunction

- To stop or prevent actions that lead to violation of the law
  - e.g., manufacturing practices that may lead to the introduction of violative products into interstate commerce
- To correct the conditions that caused the violation to occur
- An order issued by the Court in which one or more defendant is ordered to do and/or refrain from doing a specified act or acts

Reasons for Injunction

- Significant out-of-compliance circumstances
  - Repeated violations
  - Types of violations (e.g., system-wide problems)
- Does not preclude additional or concurrent action
  - Recall
  - Public information
  - Seizure
  - License suspension/revocation
  - Criminal prosecution